

Applicants : Douglas J. M. Allen, et al.
Serial No. : Not Yet Known
November 17, 2003 Preliminary Amendment
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In the Specification

Please amend the title appearing on page 1, line 5 as follows:

-- N-(3-ETHYNYLPHENYLAMINO)-6,7-BIS(2-METHOXYETHOXY)-4-
QUINAZOLINAMINE MESYLATE ANYHDRATE AND MONOHYDRATE --

Please insert the following paragraph beginning on page 1 after the title as follows:

-- This application is a continuation of U.S. Serial No. 09/355,534, filed July 29, 1999, now allowed, which is a §371 national stage of PCT International Application No. PCT/IB99/00612, filed April 8, 1999, claiming priority of U.S. Provisional Application No. 60/083,441, filed April 29, 1998. --

Please amend the paragraph appearing on page 1, lines 11-21 as follows:

-- United States patent application number ~~08/653,786~~ 5,747,498, ~~filed May 28, 1996~~ issued May 5, 1998, which is incorporated herein by reference in its entirety, refers to [6,7-bis(2-methoxyethoxy)-quinazolin-4-yl]-(3-ethynylphenyl)amine hydrochloride which, the patent ~~application~~ discloses, is an inhibitor of the erbB family of oncogenic and protooncogenic protein tyrosine kinases, such as epidermal growth factor receptor (EGFR), and is therefore useful for the treatment of proliferative disorders, such as cancers, in humans. The mesylate compounds of the present invention are similarly useful for the treatment of proliferative disorders, but they also possess certain advantages over the foregoing hydrochloride compound. One advantage is that the mesylate

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compounds of the present invention are more soluble in aqueous compositions than the above hydrochloride compound, and thus the mesylate compounds of the present invention are easily delivered according to parenteral methods of administration. --

Please amend the paragraph appearing on page 3, lines 19-26 as follows:

-- N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride may be prepared as described in United States patent application number 08/653,786 5,747,498, ~~filed May 28, 1996~~ issued May 5, 1998, referred to above. N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine mesylate monohydrate may be prepared by mixing N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)-4-quinazolinamine hydrochloride in ethyl acetate and water, warming the mixture to a temperature of about 60-70°C, adding sodium hydroxide to adjust the pH to within a range of about 10-11, separating the organic ethyl acetate phase, and then adding methanesulfonic acid to the organic phase to provide the mesylate monohydrate. --